

Appl. No.: 10/510,120  
Amdt. dated 05/08/2006  
Reply to Office action of December 6, 2005

**REMARKS/ARGUMENTS**

Applicants have amended claim 1 to recite "reductively deoxygenating the C-3' amide group on the taxane molecule to form an a C-3' imine compound." Applicants have amended claim 2 to include the word "contacting" rather than "conducting". Applicants have amended claim 16 to correct an error in the order of the formulas provided in that claim. This amendment is supported by the specification including pages 14-15. Applicants have amended claim 21 to correct a typographical error by replacing the word "amine" with "imine," and this amendment is supported by the specification including original claims 16 and 20 and pages 20-21. Applicants amended claims 13, 26, and 38 to correct several typographical errors, and these amendments are supported by the specification, including page 19. Applicants have amended claim 40 to recite the language "an amide group on" and "to effect acyl migration," and this amendment is supported by the specification, including page 21. Applicants respectfully submit that no new matter has been introduced by these amendments and that these claims are fully supported throughout the specification and by the original claims. Applicants respectfully request entry of these amendments. Claims 1-43 are currently pending.

**35 U.S.C. § 112 Rejections**

Claims 1-43 stand rejected under 35 U.S.C. § 112 as "vague and unclear as to the final product." As noted above, the chemical structures provided in claim 16 have been corrected to provide them in the correct order in the claim. Applicants note that the structures and claim steps in claims 1 and 16 as currently pending make it clear to one skilled in the art that the second taxane structure as provided in claims 1 and 16 is the product of reacting the first taxane structure as provided in claims 1 and 16 using the steps as provided in the respective claims. The diagram provided by the examiner in the present Office Action is correct except that the original reactant amide should have R-C rather than R<sub>N</sub>-C.

The examiner has objected to the language "deoxygenating the taxane" as provided in claims 1, 2, 40 and 41. Claims 1, 2, 40, and 41 are currently amended to clarify that the

Appl. No.: 10/510,120  
Amdt. dated 05/08/2006  
Reply to Office action of December 6, 2005

deoxygenated group is the amide group, as reflected in the specification. Applicants respectfully request withdrawal of this rejection.

The examiner has also objected to the language "hindered base to form another taxane molecule" as provided in claims 1 and 40. In view of the specification and the general use of the term in the art, one skilled in the art would understand that a "hindered base" refers to a base that facilitates acyl migration that does not adversely affect other functionality present on the taxane molecule, as described on page 21 of the specification. Applicants respectfully request withdrawal of this rejection.

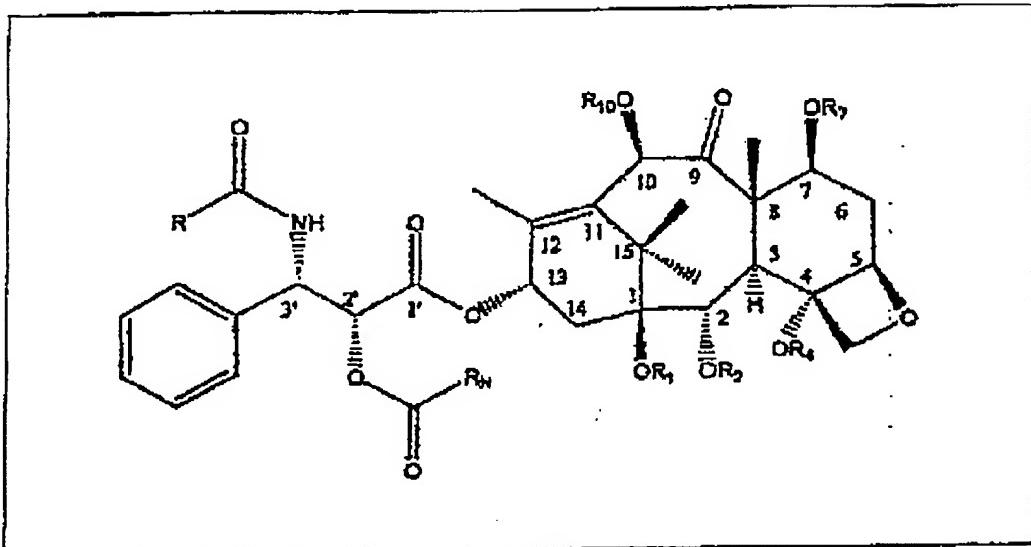
#### 35 U.S.C. § 102 Rejection

Claim 40 stands rejected under 35 U.S.C. § 102 as anticipated by U.S. Patent No. 5,679,807 to Murray, et al. The '807 patent does not disclose or suggest a method of converting an acyl protected taxane molecule comprising treating the primary amine compound with a hindered base to effect acyl migration and form another taxane molecule, as is currently claimed in claim 40. In Fig. 4 of the '807 patent, the original taxane molecule may include a protecting group is removed during the second reaction, but the protecting group in the '807 patent does not migrate to another position on the taxane molecule to form another taxane molecule. The '807 patent does not disclose or suggest acyl migration as claimed in current claim 40. Therefore, Applicants respectfully request withdrawal of this rejection.

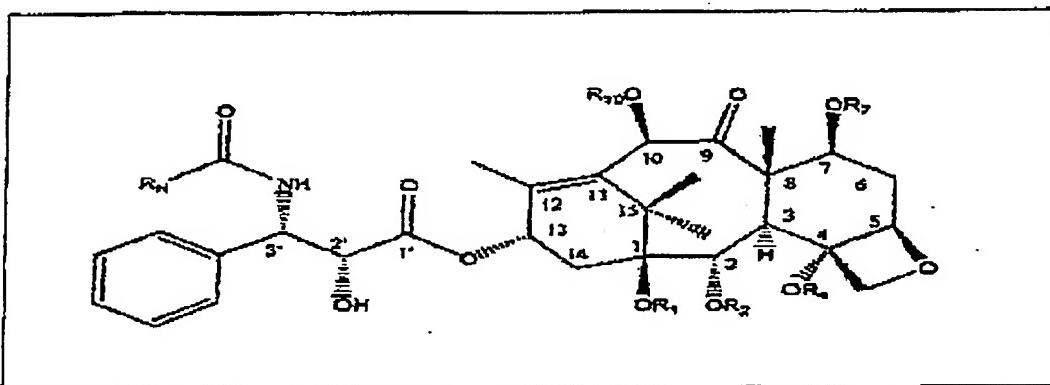
#### 35 U.S.C. § 103 Rejections

Claims 1-15 and 39-40 stand rejected under 35 U.S.C. § 103(a) as obvious in view of U.S. Patent No. 5,679,807 and U.S. Patent No. 5,808,113 both to Murray, et al. (collectively "Murray"). Figures 4-6 and the accompanying text of the Murray do not teach or suggest a method with a starting taxane molecule of

Appl. No.: 10/510,120  
 Amdt. dated 05/08/2006  
 Reply to Office action of December 6, 2005



and a resulting taxane molecule of



as claimed in claims 1-15 and 39. Specifically, the original taxane in Fig. 5 of Murray does not include the acyl group (-O-R<sub>N</sub>) or any protecting group in the 2'-O position. The original taxane in Fig. 4 of Murray includes a protecting group in the 2'-O position, but that protecting group is removed from the taxane in the second step of the reaction (deprotection). Murray does not indicate that a protecting group originating at the 2'-O position in the first taxane molecule would result in a molecule with the same protecting group at the 3'-N position in the resulting molecule. Furthermore, Murray does not disclose or suggest an acyl group originating in the 2'-

Appl. No.: 10/510,120  
Amdt. dated 05/08/2006  
Reply to Office action of December 6, 2005

O position. Likewise, Murray does not disclose or suggest a method of converting an acyl protected taxane molecule comprising treating the primary amine compound with a hindered base to effect acyl migration and form another taxane molecule, as claimed in claim 40.

Therefore, Applicants respectfully request withdrawal of this rejection.

Claims 16-39 stand rejected under 35 U.S.C. § 103(a) as obvious in view of U.S. Patent No. 5,319,112 to Kingston, et al. Kingston does not disclose or suggest the steps of "reacting the taxane molecule with zirconocene chloride hydride in a solvent to form an imine compound" and "hydrolyzing the imine compound to form a primary amine compound" as claimed in current claims 16-39. To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the reference, (2) there must be a reasonable expectation of success, and (3) the prior art reference must teach or suggest all the claim limitations. MPEP 2142 and 2143. Kingston does not (3) teach or suggest the specific steps as claimed in claims 16-39, as noted above.

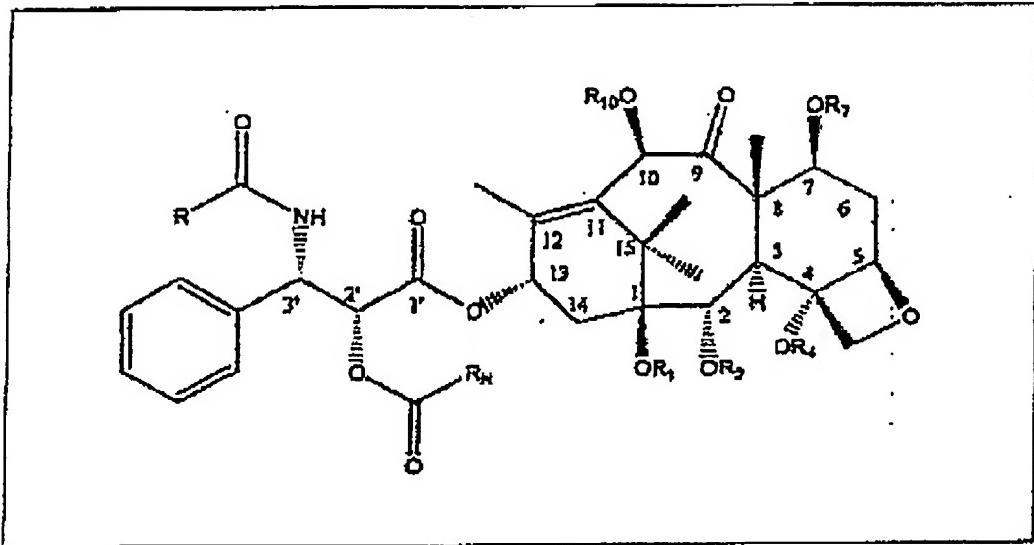
Kingston also does not (1) provide any suggestion or motivation to modify the reaction indicated in Kingston. While the Office Action indicates "One having ordinary skill in the art would have been motivated to modify the process of changing the reagents. Because changing from one reagent to another is within the skill of the Ordinary Artisan," such a statement does not fulfill the factual requirements for *prima facie* obviousness. Being within the skill of the Ordinary Artisan is not sufficient to provide motivation to modify the reference. See MPEP 2143.01 (IV). Even if a skilled artisan would have been motivated by Kingston to change the process steps and reagents, Kingston provides no expectation of success (2). The formation of the primary amine in Kingston is a fundamentally different reaction using different reagents than the reaction steps claimed in claims 16-39. Applicants respectfully request withdrawal of this rejection.

Appl. No.: 10/510,120  
Amdt. dated 05/08/2006.  
Reply to Office action of December 6, 2005

Claims 1-15 and 39-40 stand rejected under 35 U.S.C. § 103(a) as obvious in view of U.S. Patent No. 5,760,251 and WO 97/07110 both to Gao, et al. (collectively "Gao"). As with Kingston above, Gao does not teach or suggest the specific steps as claimed in claims 1-15, 39, and 40, nor does it provide any suggestion or motivation to modify the reaction indicated therein as is required for *prima facie* obviousness. The generic reference to "cleaving" the  $\beta$ -alkoxycarbonyl- in Gao does not render obvious the specific method steps as claimed in claims 1-15 and 39-40. Gao does not disclose or suggest any of the steps of "reductively deoxygenating the C-3' amide group on the taxane molecule to form an a C-3' imine compound;" "hydrolyzing the imine compound to form a primary amine compound;" and "treating the primary amine compound with a base to form another taxane molecule" as claimed in claims 1-15 and 39. Gao also does not disclose or suggest any of the steps of "reductively deoxygenating an amide group on the taxane molecule to form an imine compound;" "hydrolyzing the imine compound to form a primary amine compound;" and "treating the primary amine compound with a hindered base to effect acyl migration and form another taxane molecule" as claimed in current claim 40. Applicants respectfully request withdrawal of this rejection.

Claims 16-39 stand rejected under 35 U.S.C. § 103(a) as obvious in view of U.S. Patent No. 6,531,611 to Schloemer, et al. Schloemer does not include the same starting taxane molecule structure as claimed in current claims 16-39, even as an intermediary, nor does it disclose or suggest any of the process steps as claimed in claims 16-39, and therefore addresses a different reaction altogether. The compound of formula 7 in Schloemer does not correspond to the structure:

Appl. No.: 10/510,120  
 Amdt. dated 05/08/2006  
 Reply to Office action of December 6, 2005



as claimed in current claims 16-39, as there is no 2'O acyl group. Schloemer also does not disclose or suggest any of the steps of "reacting the taxane molecule with zirconocene chloride hydride in a solvent to form an imine compound;" "hydrolyzing the imine compound to form a primary amine compound" and "treating the primary amine compound with a base to form another taxane molecule" as claimed in current claims 16-39. Like Kingston and Gao, Schloemer discloses a different reaction using different reagents than the reaction steps claimed in claims 16-39. Applicants respectfully request withdrawal of this rejection.

Consideration Of Previously Submitted Information Disclosure Statement

It is noted that an initialed copy of the PTO Form 1449 that was submitted with Applicants' Information Disclosure Statement filed August 15, 2005 has not been returned to Applicants' representative with the Office Action. Accordingly, it is requested that an initialed copy of the Form 1449 be forwarded to the undersigned with the next communication from the PTO. In order to facilitate review of the references by the Examiner, a copy of the Information Disclosure Statement and the Form 1449 are attached hereto. Copies of the cited references were provided at the time of filing the original Information Disclosure Statement, and therefore no

Appl. No.: 10/510,120  
Amdt. dated 05/08/2006  
Reply to Office action of December 6, 2005

additional copies of the references are submitted herewith. Applicants will be pleased to provide additional copies of the references upon the Examiner's request.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



Cynthia V. Hall  
Registration No. 56,544

Customer No. 00826  
**ALSTON & BIRD LLP**  
Bank of America Plaza  
101 South Tryon Street, Suite 4000  
Charlotte, NC 28280-4000  
Tel Atlanta Office (404) 881-7000  
Fax Atlanta Office (404) 881-7777

**CERTIFICATION OF FACSIMILE TRANSMISSION**  
I hereby certify that this paper is being facsimile transmitted to the US Patent and Trademark Office at Fax No. (571) 273-8300 on the date shown below.

  
\_\_\_\_\_  
Lori Goldstein

5/8/06  
\_\_\_\_\_  
Date